# Complete Summary

## GUIDELINE TITLE

Chronic kidney disease. Early identification and management of chronic kidney disease in adults in primary and secondary care.

## BIBLIOGRAPHIC SOURCE(S)

National Collaborating Centre for Chronic Conditions. Chronic kidney disease. Early identification and management of chronic kidney disease in adults in primary and secondary care. London (UK): National Institute for Health and Clinical Excellence (NICE); 2008 Sep. 36 p. (Clinical guideline; no. 73).

## GUIDELINE STATUS

This is the current release of the guideline.

## COMPLETE SUMMARY CONTENT



## SCOPE

### DISEASE/CONDITION(S)

Chronic kidney disease (CKD)

### GUIDELINE CATEGORY

Assessment of Therapeutic Effectiveness
Counseling
Diagnosis
Evaluation
Management
Prevention

Risk Assessment
Treatment

## CLINICAL SPECIALTY

Cardiology
Endocrinology
Family Practice
Internal Medicine
Nephrology
Preventive Medicine

## INTENDED USERS

Advanced Practice Nurses
Clinical Laboratory Personnel
Nurses
Patients
Pharmacists
Physician Assistants
Physicians

## GUIDELINE OBJECTIVE(S)

To provide guidance on the care of adults with chronic kidney disease (CKD) by identifying:

- People who have or are at risk of developing CKD
- Those who need intervention to minimize cardiovascular risk and what that intervention should be
- Those who will develop progressive kidney disease and/or complications of kidney disease and how they can be managed
- Those who need referral for specialist kidney care

## TARGET POPULATION

Adults who have or are at risk of developing chronic kidney disease (CKD)

**Note**: The guideline does not cover children (aged under 16 years), people receiving renal replacement therapy, people with acute kidney injury (acute renal failure) and rapidly progressive glomerulonephritis, the treatment of each of the specific causes of CKD, the management of pregnancy in women with CKD, and the management of anemia in people with CKD.

## INTERVENTIONS AND PRACTICES CONSIDERED

### Diagnosis/Evaluation/Risk Assessment

1. Measurement of estimated glomerular filtration rate (eGFR)
2. Detection of blood in the urine using reagent strips
3. Detection of protein in the urine using urine albumin/creatinine ratio (ACR) (preferred) or protein/creatinine ratio (PCR)

4. Measurement of serum calcium, phosphate, and parathyroid hormone (PTH) concentrations in people with stage 4 or 5 chronic kidney disease (CKD)
5. Hemoglobin level measurement to identify anemia in people with stage 3B, 4 or 5 CKD
6. Renal ultrasound if indicated

**Note**: Routine measurement of calcium, phosphate, PTH, and vitamin D levels in people with stage 1, 2, 3A or 3B CKD was considered but not recommended.

### Management/Treatment/Prevention

1. Patient education about the stages and causes of CKD, the associated complications, and the risk of progression
2. Specialist referral
3. Lifestyle advice
4. Pharmacotherapy
    - Blood pressure control (angiotensin-converting enzyme [ACE] inhibitors or angiotensin receptor blockers [ARBs])
    - Statins
    - Antiplatelet drugs
    - Bisphosphonates
    - Vitamin D (cholecalciferol, ergocalciferol, alfacalcidol, calcitriol)

**Note**: Use of spironolactone and routine use of drugs to lower uric acid were considered but not recommended

## MAJOR OUTCOMES CONSIDERED

- Clinical effectiveness
    - Sensitivity, specificity, and accuracy of diagnostic tests
    - Changes in glomerular filtration rate, serum creatinine, and protein excretion
    - Progression to end stage renal disease
    - Major cardiovascular events
    - All-cause and cardiovascular mortality
- Cost-effectiveness

# METHODOLOGY

## METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

## DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

**Note from the National Guideline Clearinghouse**: The guideline was developed by the National Collaborating Centre for Chronic Conditions (NCC-CC) on behalf of the National Institute for Health and Excellence (NICE). See the "Availability of Companion Documents" field for the full version of this guideline.

### Searching for the Evidence

The information scientist developed a search strategy for each question. Key words for the search were identified by the GDG. In addition, the health economist searched for additional papers providing economics evidence or to inform detailed health economics work (for example, modelling). Papers that were published or accepted for publication in peer-reviewed journals were considered as evidence by the GDG. Conference paper abstracts and non-English language papers were excluded from the searches.

Each clinical question dictated the appropriate study design that was prioritised in the search strategy but the strategy was not limited solely to these study types. The research fellow or health economist identified relevant titles and abstracts from the search results for each clinical question and full papers were obtained. Exclusion lists were generated for each question together with the rationale for the exclusion. The exclusion lists were presented to the GDG. See Appendix A in the full version of the original guideline document (see the "Availability of Companion Documents" field) for literature search details.

### Health Economics Evidence

Published economic evaluations were retrieved, assessed and reviewed for every guideline question. Full economic evaluations were included, that is those studies that compare the overall health outcomes of different interventions as well as their cost. Cost analyses and cost consequence analysis, which do not evaluate overall health gain, were not included. Evaluations conducted in the context of non-Organisation for Economic Co-operation and Development (OECD) countries were also excluded, since costs and care pathways are unlikely to be transferrable to the UK National Health Service (NHS).

## NUMBER OF SOURCE DOCUMENTS

Not stated

## METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus
Weighting According to a Rating Scheme (Scheme Given)

## RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

### Levels of Evidence for Intervention Studies

**1++** High-quality meta-analyses, systematic reviews of randomized controlled trials (RCTs), or RCTs with a very low risk of bias

**1+** Well-conducted meta-analyses, systematic reviews of RCTs or RCTs with a low risk of bias

**1–** Meta-analyses, systematic reviews of RCTs or RCTs with a high risk of bias*

**2++** High-quality systematic reviews of case–control or cohort studies

High quality case–control or cohort studies with a very low risk of confounding, bias or chance and a high probability that the relation is causal

**2+** Well-conducted case–control or cohort studies with a very low risk of confounding, bias or chance and a moderate probability that the relation is causal

**2–** Case–control or cohort studies with a high risk of confounding, bias or chance and a significant risk that the relationship is not causal*

**3** Non-analytic studies (for example, case reports, case series)

**4** Expert opinion, formal consensus

*Studies with a level of evidence '–' should not be used as a basis for making a recommendation.

## METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review with Evidence Tables

## DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

**Note from the National Guideline Clearinghouse**: The guideline was developed by the National Collaborating Centre for Chronic Conditions (NCC-CC) on behalf of the National Institute for Health and Excellence (NICE). See the "Availability of Companion Documents" field for the full version of this guideline.

### Appraising the Evidence

The research fellow or health economist, as appropriate, critically appraised the full papers. In general, no formal contact was made with authors however there were *ad hoc* occasions when this was required in order to clarify specific details. Critical appraisal checklists were compiled for each full paper. One research fellow undertook the critical appraisal and data extraction. The evidence was considered carefully by the GDG for accuracy and completeness.

### Health Economics Evidence

Published economic evaluations were retrieved, assessed and reviewed for every guideline question. Full economic evaluations were included, that is those studies that compare the overall health outcomes of different interventions as well as their cost. Cost analyses and cost consequence analysis, which do not evaluate overall health gain, were not included. Evaluations conducted in the context of non-OECD countries were also excluded, since costs and care pathways are unlikely to be transferrable to the UK National Health ServiceÂ (NHS).

Areas for health economics modelling were agreed by the GDG after the formation of the clinical questions. The health economist reviewed the clinical questions to consider the potential application of health economics modelling, and these priorities were agreed with the GDG. The health economist performed supplemental literature searches to obtain additional data for modelling.

Assumptions, data and structures of the models were explained to and agreed by the GDG members during meetings, and they commented on subsequent revisions.

### Distilling and Synthesising the Evidence and Developing Recommendations

The evidence from each full paper was distilled into an evidence table and synthesised into evidence statements before being presented to the GDG. This evidence was then reviewed by the GDG and used as a basis upon which to formulate recommendations. The criteria for grading evidence is shown in the "Rating Scheme for the Strength of the Evidence." field.

Evidence tables are available online at the Royal College of Physicians Web site.

## METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

## DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

**Note from the National Guideline Clearinghouse (NGC)**: The guideline was developed by the National Collaborating Centre for Chronic Conditions (NCC-CC) on behalf of the National Institute for Health and Excellence (NICE). See the "Availability of Companion Documents" field for the full version of this guideline.

### The Guideline Development Group (GDG)

The GDG met monthly (January 2007 to February 2008) and comprised a multidisciplinary team of health professionals and people with chronic kidney disease, who were supported by the technical team.

The GDG membership details including patient representation and professional groups are detailed in the GDG membership table at the front of the full version of the original guideline document (see the "Availability of Companion Documents" field).

### Guideline Project Executive (PE)

The PE was involved in overseeing all phases of the guideline.

It also reviewed the quality of the guideline and compliance with the Department of Health (DH) remit and NICE scope.

The PE comprised of:

- NCC-CC Director
- NCC-CC Assistant Director
- NCC-CC Manager
- NICE Commissioning Manager

- Technical Team

**Formal Consensus**

At the end of the guideline development process the GDG met to review and agree the guideline recommendations.

**The Process of Guideline Development**

The basic steps in the process of producing a guideline are:

- Developing clinical questions
- Systematically searching for the evidence
- Critically appraising the evidence
- Incorporating health economics evidence
- Distilling and synthesising the evidence and writing recommendations
- Grading the evidence statements
- Agreeing the recommendations
- Structuring and writing the guideline
- Updating the guideline

*Developing Evidence-Based Questions*

The technical team drafted a series of clinical questions that covered the guideline scope. The GDG and Project Executive refined and approved these questions, which are shown in Appendix A of the full version of the original guideline document (see the "Availability of Companion Documents" field).

*Agreeing the Recommendations*

The GDG employed formal consensus techniques to:

- Ensure that the recommendations reflected the evidence base
- Approve recommendations based on lesser evidence or extrapolations from other situations
- Reach consensus recommendations where the evidence was inadequate
- Debate areas of disagreement and finalise recommendations

The GDG also reached agreement on:

- Recommendations as key priorities for implementation
- Key research recommendations
- Algorithms

*Writing the Guideline*

The first draft version of the guideline was drawn up by the technical team in accordance with the decisions of the GDG, incorporating contributions from individual GDG members in their expert areas and edited for consistency of style and terminology. The guideline was then submitted for a formal public and stakeholder consultation prior to publication. The registered stakeholders for this

guideline are detailed on the NICE website, www.nice.org.uk. Editorial responsibility for the full guideline rests with the GDG. The different versions of the guideline are shown in Table 2.3 of the full version of the original guideline document (see the "Availability of Companion Documents" field).

## RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

## COST ANALYSIS

The cost-effectiveness analysis showed that urinary albumin/creatinine ratio (ACR) (performed in a hospital laboratory) was more cost-effective than the use of protein or albumin reagent strips. In a sensitivity analysis, the Guideline Development Group (GDG) found that ACR has to be only very slightly more accurate than protein/creatinine ratio (PCR) for ACR to be cost-effective across a range of plausible cost differentials.

### Original Modelling: Non-Diabetic Hypertensive

The base case analysis showed that one-off testing of hypertensive adults at various ages is highly cost-effective. The initial use of ACR is more cost-effective than ACR after a positive reagent strip test. ACR is likely to be more cost-effective than PCR as long as it is sensitive enough to pick up 1% more cases than the PCR test. The results were not sensitive to any individual model parameter. Although the results were not sensitive to the individual treatment effect of angiotensin-converting enzyme inhibitor (ACEI) on progression or the effect of ACEI on mortality, when both parameters were covaried, testing was not always cost-effective.

### Original Modelling: Non-Diabetic, Non-Hypertensive

The base case analysis showed that testing of non-hypertensive, non-diabetic adults at ages 55 to 79 is not cost-effective. However, at age 80, testing appeared to be cost-effective.

The cost-effectiveness evidence suggests that testing for chronic kidney disease (CKD) in high-risk groups (such as those with hypertension or diabetes) is highly cost-effective. However, for over 55s without additional risk factors, the prevalence of CKD with proteinuria was too low for testing to be cost-effective.

All of the economic evaluations of angiotensin-converting enzyme (ACE) inhibitors found that these drugs confer both health gains and net cost-savings compared with conventional (non-ACE inhibitor) therapy (i.e., they are dominant therapies).

Refer to Appendix C in the full version of the original guideline document for details on cost analyses (see the "Availability of Companion Documents" field).

## METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

### DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

The guideline was validated through two consultations.

1. The first draft of the guideline (The full guideline, National Institute for Clinical Excellence [NICE] guideline and Quick Reference Guide) were consulted with Stakeholders and comments were considered by the Guideline Development Group (GDG)
2. The final consultation draft of the Full guideline, the NICE guideline and the Information for the Public were submitted to stakeholders for final comments.

The final draft was submitted to the Guideline Review Panel for review prior to publication.

## RECOMMENDATIONS

### MAJOR RECOMMENDATIONS

**Note from the National Guideline Clearinghouse (NGC)**: The guideline was developed by the National Collaborating Centre for Chronic Conditions (NCC-CC) on behalf of the National Institute for Health and Excellence (NICE). See the "Availability of Companion Documents" field for the full version of this guideline.

**Investigation**

**Measurement of Kidney Function**

- Whenever a request for serum creatinine measurement is made, clinical laboratories should report an estimate of glomerular filtration rate (eGFR) using a prediction equation (see the recommendation below) in addition to reporting the serum creatinine result.Â  (Note: eGFR may be less reliable in certain situations [for example, acute renal failure, pregnancy, oedematous states, muscle wasting disorders, amputees and malnourished people] andÂ hasÂ notÂ beenÂ wellÂ validated in certain ethnic groups [for example, Asians and Chinese]).
- Use the isotope dilution mass spectrometry (IDMS)-traceable simplified modification of diet in renal disease (MDRD) equation to estimate GFR, using creatinine assays with calibration traceable to a standardised reference material. Ideally use creatinine assays that are specific and zero biased compared with IDMS (for example, enzymatic assays). When non-specific assays are used (for example, Jaffe assays), employ appropriate assay-specific adjustment factors to minimise between-laboratory variation (for example, those provided by national external quality assessment schemes).
- Where indicated, apply a correction factor for ethnicity to reported GFR values (multiply eGFR by 1.21 for African-Caribbean ethnicity). (In practice this correction factor should also be applied to those of African ethnicity).

- Interpret reported values of eGFR 60 mL/min/1.73 $m^2$ or more with caution, bearing in mind that estimates of GFR become less accurate as the true GFR increases.
- Where eGFR is simply reported as 60 mL/min/1.73 $m^2$ or more, use a rise in serum creatinine concentration of more than 20% to infer significant reduction in renal function.
- Where a highly accurate measure of GFR is required – for example, during monitoring of chemotherapy and in the evaluation of renal function in potential living donors – consider a gold standard measure (inulin, $^{51}$Cr-EDTA, $^{125}$I-iothalamate or iohexol).
- In cases where there are extremes of muscle mass – for example, in bodybuilders, amputees or people with muscle wasting disorders – interpret the eGFR with caution. (Reduced muscle mass will lead to overestimation and increased muscle mass to underestimation of the GFR.)
- Advise people not to eat any meat in the 12 hours before having a blood test for GFR estimation. Avoid delaying the despatch of blood samples to ensure that they are received and processed by the laboratory within 12 hours of venipuncture.
- An eGFR result less than 60 mL/min/1.73 $m^2$ in a person not previously tested should be confirmed by repeating the test within 2 weeks. Make an allowance for biological and analytical variability of serum creatinine (± 5%) when interpreting changes in eGFR.

| **Measurement of eGFR: How Often?*** | | |
|---|---|---|
| Annually in all at risk groups | | |
| During intercurrent illness and perioperatively in all patients with chronic kidney disease (CKD) | | |
| Exact frequency should depend on the clinical situation.Â  The frequency of testing may be reduced where eGFR levels remain very stable but will need to be increased if there is rapid progression. | | |
| **Stage** | **eGFR Range (ml/min/1.73m$^2$)** | **Typical Testing Frequency** |
| 1 and 2 | =60 + other evidence of kidney disease | 12 monthly |
| 3A and 3B | 30-59 | 6 monthly |
| 4 | 15-29 | 3 monthly |
| 5 | ?15 | 6 weekly |

*The information in this table is based on Guideline Development Group (GDG) consensus and not on evidence.

**Proteinuria**

Albumin is the principal component of proteinuria in glomerular disease. Reagent strips in current clinical practice predominantly detect albumin, not total protein, but are not reliably quantitative. Albumin/creatinine ratio (ACR) has far greater sensitivity than protein/creatinine ratio (PCR) for the detection of low levels of proteinuria and enhances early identification of CKD. However, there may be

clinical reasons for a specialist to subsequently use PCR to quantify and monitor significant levels of proteinuria.

- Do not use reagent strips to identify proteinuria unless they are capable of specifically measuring albumin at low concentrations and expressing the result as an ACR.
- To detect and identify proteinuria, use urine ACR in preference, as it has greater sensitivity than PCR for low levels of proteinuria. For quantification and monitoring of proteinuria, PCR can be used as an alternative. ACR is the recommended method for people with diabetes.
- For the initial detection of proteinuria, if the ACR is 30 mg/mmol or more (this is approximately equivalent to PCR 50 mg/mmol or more, or a urinary protein excretion 0.5 g/24 hoursÂ [h] or more) and less than 70 mg/mmol (approximately equivalent to PCR less than 100 mg/mmol, or urinary protein excretion less than 1 g/24 h) this should be confirmed by a subsequent early morning sample. If the initial ACR is 70 mg/mmol or more, or the PCR 100 mg/mmol or more, a repeat sample need not be tested.
- In people without diabetes consider clinically significant proteinuria to be present when the ACR is 30 mg/mmol or more (this is approximately equivalent to PCR 50 mg/mmol or more, or a urinary protein excretion 0.5 g/24 h or more).
- In people with diabetes consider microalbuminuria (ACR more than 2.5 mg/mmol in men and ACR more than 3.5 mg/mmol in women) to be clinically significant.
- All people with diabetes, and people without diabetes with a GFR less than 60 mL/min/1.73 $m^2$, should have their urinary albumin/protein excretion quantified. The first abnormal result should be confirmed on an early morning sample (if not previously obtained).
- Quantify by laboratory testing the urinary albumin/protein excretion of people with an eGFR 60 mL/min/1.73 $m^2$ or more if there is a strong suspicion of CKD.

**Haematuria**

- When testing for the presence of haematuria, use reagent strips rather than urine microscopy.
    - Evaluate further if there is a result of 1+ or more.
    - Do not use urine microscopy to confirm a positive result.
- When there is the need to differentiate persistent invisible haematuria in the absence of proteinuria from transient haematuria, regard two out of three positive reagent strip tests as confirmation of persistent invisible haematuria.
- Persistent invisible haematuria, with or without proteinuria, should prompt investigation for urinary tract malignancy in appropriate age groups.
- Persistent invisible haematuria in the absence of proteinuria should be followed up annually with repeat testing for haematuria, proteinuria/albuminuria (see recommendations above), GFR and blood pressure monitoring as long as the haematuria persists.

**Early Identification**

- Monitor GFR in people prescribed drugs known to be nephrotoxic such as calcineurin inhibitors and lithium. Check GFR at least annually in people

receiving long-term systemic non-steroidal anti-inflammatory drug (NSAID) treatment.

- Offer people testing for CKD if they have any of the following risk factors:
    - Diabetes
    - Hypertension
    - Cardiovascular disease (ischaemic heart disease, chronic heart failure, peripheral vascular disease and cerebral vascular disease)
    - Structural renal tract disease, renal calculi or prostatic hypertrophy
    - Multisystem diseases with potential kidney involvement – for example, systemic lupus erythematosus
    - Family history of stage 5 CKD or hereditary kidney disease
    - Opportunistic detection of haematuria or proteinuria
- In the absence of the above risk factors, do not use age, gender or ethnicity as risk markers to test people for CKD. In the absence of metabolic syndrome, diabetes or hypertension, do not use obesity alone as a risk marker to test people for CKD.

## Classification

- Use the suffix (p) to denote the presence of proteinuria when staging CKD.
- For the purposes of this classification define proteinuria as urinary ACR 30 mg/mmol or more, or PCR 50 mg/mmol or more (approximately equivalent to urinary protein excretion 0.5 g/24 h or more).
- Stage 3 CKD (refer to the original guideline document for the description of stages of CKD) should be split into two subcategories defined by:
    - GFR 45–59 mL/min/1.73 $m^2$ (stage 3A)
    - GFR 30–44 mL/min/1.73 $m^2$ (stage 3B)
- At any given stage of CKD, management should not be influenced solely by age. (Note: In people aged over 70 years, an eGFR in the range 45–59 mL/min/1.73 $m^2$ if stable over time and without any other evidence of kidney damage, is unlikely to be associated with CKD-related complications.)

## Information and Education

- Offer people with CKD education and information tailored to the stage and cause of CKD, the associated complications and the risk of progression.
- When developing information or education programmes, involve people with CKD in their development from the outset. The following topics are suggested.
    - What is CKD and how does it affect people?
    - What questions should people ask about their kidneys when they attend clinic?
    - What treatments are available for CKD, what are their advantages and disadvantages and what complications or side effects may occur as a result of treatment/medication?
    - What can people do to manage and influence their own condition?
    - In what ways could CKD and its treatment affect people's daily life, social activities, work opportunities and financial situation, including benefits and allowances available?
    - How can people cope with and adjust to CKD and what sources of psychological support are available?

    - When appropriate, offer information about renal replacement therapy (such as the frequency and length of time of dialysis treatment sessions or exchanges and pre-emptive transplantation) and the preparation required (such as having a fistula or peritoneal catheter).
    - Conservative management may be considered where appropriate.
- Offer people with CKD high quality information or education programmes at appropriate stages of their condition to allow time for them to fully understand and make informed choices about their treatment.
- Healthcare professionals providing information and education programmes should ensure they have specialist knowledge about CKD and the necessary skills to facilitate learning.
- Healthcare professionals working with people with CKD should take account of the psychological aspects of coping with the condition and offer access to appropriate support – for example, support groups, counselling or a specialist nurse.

**Indications for Renal Ultrasound**

- Offer a renal ultrasound to all people with CKD who:
    - Have progressive CKD (eGFR decline more than 5 mL/min/1.73 $m^2$ within 1 year, or more than 10 mL/min/1.73 $m^2$ within 5 years)
    - Have visible or persistent invisible haematuria
    - Have symptoms of urinary tract obstruction
    - Have a family history of polycystic kidney disease and are aged over 20
    - Have stage 4 or 5 CKD
    - Are considered by a nephrologist to require a renal biopsy
- Advise people with a family history of inherited kidney disease about the implications of an abnormal result before a renal ultrasound scan is arranged for them.

**Progression**

- Take the following steps to identify progressive CKD:
    - Obtain a minimum of three GFR estimations over a period of not less than 90 days.
    - In people with a new finding of reduced eGFR, repeat the eGFR within 2 weeks to exclude causes of acute deterioration of GFR – for example, acute kidney injury or initiation of angiotensin-converting enzyme (ACE) inhibitor/angiotensin receptor blockers (ARB) therapy.
    - Define progression as a decline in eGFR of more than 5 mL/min/1.73 $m^2$ within 1 year, or more than 10 mL/min/1.73 $m^2$ within 5 years.
    - Focus particularly on those in whom a decline of GFR continuing at the observed rate would lead to the need for renal replacement therapy within their lifetime by extrapolating the current rate of decline.
- Work with people who have risk factors for progression of CKD to optimise their health. These risk factors are:
    - Cardiovascular disease
    - Proteinuria
    - Hypertension
    - Diabetes
    - Smoking

    - Black or Asian ethnicity
    - Chronic use of NSAIDs
    - Urinary outflow tract obstruction
- In people with CKD the chronic use of NSAIDs may be associated with progression and acute use is associated with a reversible fall in GFR. Exercise caution when treating people with CKD with NSAIDs over prolonged periods of time. Monitor the effects on GFR, particularly in people with a low baseline GFR and/or in the presence of other risks for progression.

## Referral Criteria

- People with CKD in the following groups should normally be referred for specialist assessment:
    - Stage 4 and 5 CKD (with or without diabetes)
    - Higher levels of proteinuria (ACR 70 mg/mmol or more, approximately equivalent to PCR 100 mg/mmol or more, or urinary protein excretion 1 g/24 h or more) unless known to be due to diabetes and already appropriately treated
    - Proteinuria (ACR 30 mg/mmol or more, approximately equivalent to PCR 50 mg/mmol or more, or urinary protein excretion 0.5 g/24 h or more) together with haematuria
    - Rapidly declining eGFR (more than 5 mL/min/1.73 $m^2$ in 1 year, or more than 10 mL/min/1.73 $m^2$ within 5 years)
    - Hypertension that remains poorly controlled despite the use of at least four antihypertensive drugs at therapeutic doses (see 'Hypertension: management of hypertension in adults in primary care' [NICE clinical guideline 34])
    - People with, or suspected of having, rare or genetic causes of CKD
    - Suspected renal artery stenosis
- Consider discussing management issues with a specialist by letter, email or telephone in cases where it may not be necessary for the person with CKD to be seen by the specialist.
- Once a referral has been made and a plan jointly agreed, it may be possible for routine follow-up to take place at the patient's GP surgery rather than in a specialist clinic. If this is the case, criteria for future referral or re-referral should be specified.
- Take into account the individual's wishes and comorbidities when considering referral.
- People with CKD and renal outflow obstruction should normally be referred to urological services, unless urgent medical intervention is required – for example, for the treatment of hyperkalaemia, severe uraemia, acidosis or fluid overload.

## Lifestyle Advice

- Encourage people with CKD to take exercise, achieve a healthy weight and stop smoking.
- Where the clinician in discussion with the patient has decided that dietary intervention to influence progression of CKD is indicated, an appropriately trained professional should discuss the risks and benefits of dietary protein restriction, with particular reference to slowing down the progression of disease versus protein-calorie malnutrition.

- Where dietary intervention is agreed this should occur within the context of education, detailed dietary assessment and supervision to ensure malnutrition is prevented.
- Offer dietary advice to people with progressive CKD concerning potassium, phosphate, protein, calorie and salt intake when indicated.

## Pharmacotherapy

### Blood Pressure Control

- In people with CKD, aim to keep the systolic blood pressure below 140 mmHg (target range 120–139 mmHg) and the diastolic blood pressure below 90 mmHg.

  (Note: The GDG searched for and appraised evidence on blood pressure control, and did not set out to establish definitive safe ranges of blood pressure in CKD. The evidence presented in the full version of the original guideline does not therefore include safety of low blood pressure, but some such evidence does exist. Existing hypertension guidelines such as the NICE hypertension guideline [NICE clinical guideline 34] give a range rather than just an upper limit and clinicians find this clear guidance useful. The GDG therefore set out a range of blood pressure targets, given in these recommendations, which in their clinical experience will inform good practice in CKD).

- In people with CKD and diabetes, and also in people with an ACR 70 mg/mmol or more (approximately equivalent to PCR 100 mg/mmol or more, or urinary protein excretion 1 g/24 h or more) aim to keep the systolic blood pressure below 130 mmHg (target range 120–129 mmHg) and the diastolic blood pressure below 80 mmHg.

### Choice of Antihypertensive Agents

- When implementing blockade of the renin–angiotensin system start treatment with an ACE inhibitor first then move to an ARB if the ACE inhibitor is not tolerated.
- Offer ACE inhibitors/ARBs to people with diabetes and ACR more than 2.5 mg/mmol (men) or more than 3.5 mg/mmol (women) irrespective of the presence of hypertension or CKD stage.

  (Note: Two different ACR thresholds are given here for initiating ACE inhibitor treatment in people with CKD and proteinuria. The potential benefit of ACE inhibitors in this context is greatly increased if the person also has diabetes or hypertension, and in these circumstances, a lower threshold is applied. The evidence base at present does not allow thorough analysis of all scenarios and the GDG based these decisions on clinical experience as well as what evidence there is).

- Offer ACE inhibitors/ARBs to non-diabetic people with CKD and hypertension and ACR 30 mg/mmol or more (approximately equivalent to PCR 50 mg/mmol or more, or urinary protein excretion 0.5 g/24 h or more).

- Offer ACE inhibitors/ARBs to non-diabetic people with CKD and ACR 70 mg/mmol or more (approximately equivalent to PCR 100 mg/mmol or more, or urinary protein excretion 1 g/24 h or more) irrespective of the presence of hypertension or cardiovascular disease.
- Offer non-diabetic people with CKD and hypertension and ACR less than 30 mg/mmol (approximately equivalent to PCR less than 50 mg/mmol, or urinary protein excretion less than 0.5 g/24 h) a choice of antihypertensive treatment according to the NICE guidance on hypertension (NICE clinical guideline 34) to prevent or ameliorate progression of CKD.
- When using ACE inhibitors/ARBs titrate them to the maximum tolerated therapeutic dose before adding a second-line agent. (There is insufficient evidence to recommend the routine use of spironolactone in addition to ACE inhibitor and ARB therapy to prevent or ameliorate progression of CKD).
- To improve concordance, inform people who are prescribed ACE inhibitors or ARB therapy about the importance of:
    - Achieving the optimal tolerated dose of ACE inhibitor/ARB
    - Monitoring eGFR and serum potassium in achieving this safely

**Practicalities of Treatment with ACE Inhibitors/ARBs**

- In people with CKD, measure serum potassium concentrations and estimate the GFR before starting ACE inhibitor/ARB therapy. Repeat these measurements between 1 and 2 weeks after starting ACE inhibitor/ARB therapy and after each dose increase.
- ACE inhibitor/ARB therapy should not normally be started if the pretreatment serum potassium concentration is significantly above the normal reference range (typically more than 5.0 mmol/litre).
- When hyperkalaemia precludes the use of ACE inhibitors/ARBs, assessment, investigation and treatment of other factors known to promote hyperkalaemia should be undertaken and the serum potassium concentration rechecked.
- Concurrent prescription of drugs known to promote hyperkalaemia is not a contraindication to the use of ACE inhibitors/ARBs, but be aware that more frequent monitoring of serum potassium concentration may be required.
- Stop ACE inhibitor/ARB therapy if the serum potassium concentration rises to 6.0 mmol/litre or more and other drugs known to promote hyperkalaemia have been discontinued.
- Following the introduction or dose increase of ACE inhibitor/ARB, do not modify the dose if either the GFR decrease from pretreatment baseline is less than 25% or the plasma creatinine increase from baseline is less than 30%.
- If there is a fall in eGFR or rise in plasma creatinine after starting or increasing the dose of ACE inhibitor/ARB, but it is less than 25% (eGFR) or 30% (serum creatinine) of baseline, the test should be repeated in a further 1–2 weeks. Do not modify the ACE inhibitor/ARB dose if the change in eGFR is less than 25% or the change in plasma creatinine is less than 30%.
- If the change in eGFR is 25% or more or the change in plasma creatinine is 30% or more:
    - Investigate other causes of a deterioration in renal function such as volume depletion or concurrent medication (for example, NSAIDs)
    - If no other cause for the deterioration in renal function is found, stop the ACE inhibitor/ARB therapy or reduce the dose to a previously tolerated lower dose, and add an alternative antihypertensive medication if required.

- Where indicated, the use of ACE inhibitors/ARBs should not be influenced by a person's age as there is no evidence that their appropriate use in older people is associated with a greater risk of adverse effects.

**Statins and Antiplatelet Drugs**

- The use of statin therapy for the primary prevention of cardiovascular disease (CVD) in people with CKD should not differ from its use in people without CKD and should be based on existing risk tables for people with and without diabetes. It should be understood that the Framingham risk tables significantly underestimate risk in people with CKD.

  (Note: There is insufficient evidence to support the routine use of statins to prevent or ameliorate progression of CKD. The use of statins for the primary prevention of CVD in people with CKD should be informed by the SHARP study (Baigent C & Landry M, 2003).

- Offer statins to people with CKD for the secondary prevention of CVD irrespective of baseline lipid values.
- Offer antiplatelet drugs to people with CKD for the secondary prevention of CVD. CKD is not a contraindication to the use of low dose aspirin but clinicians should be aware of the increased risk of minor bleeding in people with CKD given multiple antiplatelet drugs.
- There is insufficient evidence to recommend the routine use of drugs to lower uric acid in people with CKD who have asymptomatic hyperuricaemia.

**<u>Other Complications</u>**

**Bone Metabolism and Osteoporosis**

- The routine measurement of calcium, phosphate, parathyroid hormone (PTH) and vitamin D levels in people with stage 1, 2, 3A or 3B CKD is not recommended.
- Measure serum calcium, phosphate and PTH concentrations in people with stage 4 or 5 CKD (GFR less than 30 mL/min/1.73 $m^2$). Determine the subsequent frequency of testing by the measured values and the clinical circumstances. Where doubt exists seek specialist opinion.
- Offer bisphosphonates if indicated for the prevention and treatment of osteoporosis in people with stage 1, 2, 3A or 3B CKD.
- When vitamin D supplementation is indicated in people with CKD offer:
  - Cholecalciferol or ergocalciferol to people with stage 1, 2, 3A or 3B CKD
  - 1-alpha-hydroxycholecalciferol (alfacalcidol) or 1.25-dihydroxycholecalciferol (calcitriol) to people with stage 4 or 5 CKD
- Monitor serum calcium and phosphate concentrations in people receiving 1-alpha-hydroxycholecalciferol or 1.25-dihydroxycholecalciferol supplementation.

**Anaemia**

- If not already measured, check the haemoglobin level in people with stage 3B, 4 and 5 CKD to identify anaemia (Hb less than 11.0 g/dL, see the National Guideline Clearinghouse summary of the NICE guideline, Anaemia management in people with chronic kidney disease). Determine the subsequent frequency of testing by the measured value and the clinical circumstances.

### CLINICAL ALGORITHM(S)

Clinical algorithms are provided in the full version of the original guideline document for:

- Investigations and interventions at different stages of chronic kidney disease (CKD)
- Identification, diagnosis and referral of patients with CKD but without diabetes

## EVIDENCE SUPPORTING THE RECOMMENDATIONS

### REFERENCES SUPPORTING THE RECOMMENDATIONS

References open in a new window

### TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

Recommendations are based on clinical and cost effectiveness evidence, and where this is insufficient, the Guideline Development Group (GDG) used all available information sources and experience to make consensus recommendations.

## BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

### POTENTIAL BENEFITS

There is evidence that treatment can prevent or delay the progression of chronic kidney disease (CKD), reduce or prevent the development of complications, and reduce the risk of cardiovascular disease.

### POTENTIAL HARMS

#### Diagnostic Tests

Reagent strips are subject to false positive results because of patient dehydration, exercise, infection, and extremely alkaline urine. False negative results occur as a result of excessive hydration and urine proteins other than albumin.

#### Adverse Effects of Medications

- Angiotensin-converting enzyme inhibitors (ACEI) use was associated with a significant increase in the risk of cough compared to placebo.

- Angiotensin receptor blocker (ARB) or combination ACEI + ARB use were non-significantly associated with cough compared with placebo.
- Clinicians should be aware of the increased risk of minor bleeding in people with chronic kidney disease given multiple antiplatelet drugs.

## CONTRAINDICATIONS

### CONTRAINDICATIONS

Anaphylaxis and angioedema are absolute contraindications to angiotensin-converting enzyme inhibitor/angiotensin receptor blocker (ACEI/ARB) therapy, and symptomatic hypotension and severe aortic stenosis may also preclude their use.

## QUALIFYING STATEMENTS

### QUALIFYING STATEMENTS

- This guidance represents the view of the Institute, which was arrived at after careful consideration of the evidence available. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. However, the guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer and informed by the summary of product characteristics of any drugs they are considering.
- Implementation of this guidance is the responsibility of local commissioners and/or providers. Commissioners and providers are reminded that it is their responsibility to implement the guidance, in their local context, in light of their duties to avoid unlawful discrimination and to have regard to promoting equality of opportunity. Nothing in this guidance should be interpreted in a way that would be inconsistent with compliance with those duties.

## IMPLEMENTATION OF THE GUIDELINE

### DESCRIPTION OF IMPLEMENTATION STRATEGY

The Healthcare Commission assesses the performance of National Health Service (NHS) organisations in meeting core and developmental standards set by the Department of Health in 'Standards for better health', issued in July 2004. Implementation of clinical guidelines forms part of the developmental standard D2. Core standard C5 says that national agreed guidance should be taken into account when NHS organisations are planning and delivering care.

The National Institute for Health and Clinical Excellence (NICE) has developed tools to help organisations implement this guidance (listed below). These are available on the NICE website (http://guidance.nice.org.uk/CG73).

- Slides highlighting key messages for local discussion.
- Costing tools:

    - Costing report to estimate the national savings and costs associated with implementation.
    - Costing template to estimate the local costs and savings involved.
- Guide to resources, which signposts a selection of resources available from NICE, government and other national organisations.
- Audit support for monitoring local practice.

**Key Priorities for Implementation**

- To detect and identify proteinuria, use urine albumin: creatinine ratio (ACR) in preference, as it has greater sensitivity than protein:creatinine ratio (PCR) for low levels of proteinuria. For quantification and monitoring of proteinuria, PCR can be used as an alternative. ACR is the recommended method for people with diabetes.
- Offer angiotensin-converting enzyme inhibitors (ACE inhibitors)/angiotensin-II receptor blockers (ARBs) to non-diabetic people with CKD and hypertension and ACR 30 mg/mmol or more (approximately equivalent to PCR 50 mg/mmol or more, or urinary protein excretion 0.5 g/24 h or more).
- Stage 3 CKD should be split into two subcategories defined by:
    - GFR 45–59 mL/min/1.73 $m^2$ (stage 3A)
    - GFR 30–44 mL/min/1.73 $m^2$ (stage 3B)

  (Refer to the original guideline document for the description of stages of CKD).

- People with CKD in the following groups should normally be referred for specialist assessment:
    - Stage 4 and 5 CKD (with or without diabetes)
    - Higher levels of proteinuria (ACR 70 mg/mmol or more, approximately equivalent to PCR 100 mg/mmol or more, or urinary protein excretion 1 g/24 h or more) unless known to be due to diabetes and already appropriately treated
    - Proteinuria (ACR 30 mg/mmol or more, approximately equivalent to PCR 50 mg/mmol or more, or urinary protein excretion 0.5 g/24 h or more) together with haematuria
    - Rapidly declining estimate of GFR (eGFR) (more than 5 mL/min/1.73 $m^2$ in 1 year, or more than 10 mL/min/1.73 $m^2$ within 5 years)
    - Hypertension that remains poorly controlled despite the use of at least four antihypertensive drugs at therapeutic doses (see 'Hypertension: management of hypertension in adults in primary care' [NICE clinical guideline 34])
    - People with, or suspected of having, rare or genetic causes of CKD
    - Suspected renal artery stenosis
- Offer people testing for CKD if they have any of the following risk factors:
    - Diabetes
    - Hypertension
    - Cardiovascular disease (ischaemic heart disease, chronic heart failure, peripheral vascular disease and cerebral vascular disease)
    - Structural renal tract disease, renal calculi or prostatic hypertrophy
    - Multisystem diseases with potential kidney involvement – for example, systemic lupus erythematosus
    - Family history of stage 5 CKD or hereditary kidney disease

    - Opportunistic detection of haematuria or proteinuria
- Take the following steps to identify progressive CKD
    - Obtain a minimum of three GFR estimations over a period of not less than 90 days.
    - In people with a new finding of reduced eGFR, repeat the eGFR within 2 weeks to exclude causes of acute deterioration of GFR – for example, acute kidney injury or initiation of ACE inhibitor/ARB therapy.
    - Define progression as a decline in eGFR of more than 5 mL/min/1.73 $m^2$ within 1 year, or more than 10 mL/min/1.73 $m^2$ within 5 years.
    - Focus particularly on those in whom a decline of GFR continuing at the observed rate would lead to the need for renal replacement therapy within their lifetime by extrapolating the current rate of decline.
- In people with CKD aim to keep the systolic blood pressure below 140 mmHg (target range 120–139 mmHg) and the diastolic blood pressure below 90 mmHg.

### IMPLEMENTATION TOOLS

Audit Criteria/Indicators
Clinical Algorithm
Foreign Language Translations
Patient Resources
Quick Reference Guides/Physician Guides
Resources
Slide Presentation

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

## INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

### IOM CARE NEED

Living with Illness
Staying Healthy

### IOM DOMAIN

Effectiveness
Patient-centeredness

## IDENTIFYING INFORMATION AND AVAILABILITY

### BIBLIOGRAPHIC SOURCE(S)

National Collaborating Centre for Chronic Conditions. Chronic kidney disease. Early identification and management of chronic kidney disease in adults in primary and secondary care. London (UK): National Institute for Health and Clinical Excellence (NICE); 2008 Sep. 36 p. (Clinical guideline; no. 73).

## ADAPTATION

Not applicable: The guideline was not adapted from another source.

## DATE RELEASED

2008 Sep

## GUIDELINE DEVELOPER(S)

National Collaborating Centre for Chronic Conditions - National Government Agency [Non-U.S.]

## SOURCE(S) OF FUNDING

National Institute for Health and Clinical Excellence (NICE)

## GUIDELINE COMMITTEE

Guideline Development Group

## COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

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## FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

At each Guideline Development Group (GDG) meeting, all GDG members declared any potential conflict of interests.

## GUIDELINE STATUS

This is the current release of the guideline.

## GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) format from the National Institute for Health and Clinical Excellence (NICE) Web site.

## AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- Chronic kidney disease. National clinical guideline for early identification and management in adults in primary and secondary care. Full guideline. London (UK): National Institute for Health and Clinical Excellence (NICE); 2008. 204 p. (Clinical guideline; no. 73). Electronic copies: Available in Portable Document Format (PDF) format from the National Institute for Health and Clinical Excellence (NICE) Web site.
- Chronic kidney disease. Early identification and management of chronic kidney disease in adults in primary and secondary care. Quick reference guide. London (UK): National Institute for Health and Clinical Excellence; 2008 Sep. 15 p. (Clinical guideline; no. 73). Electronic copies: Available in Portable Document Format (PDF) from the NICE Web site.
- Chronic kidney disease. Costing report. Implementing NICE guidance. London (UK): National Institute for Health and Clinical Excellence; 2008 Sep. 33 p. (Clinical guideline; no. 73). Electronic copies: Available in Portable Document Format (PDF) from the NICE Web site.
- Chronic kidney disease. Costing template. Implementing NICE guidance. London (UK): National Institute for Health and Clinical Excellence; 2008. Various p. (Clinical guideline; no. 73). Electronic copies: Available in Portable Document Format (PDF) from the NICE Web site.
- Chronic kidney disease. Implementing NICE guidance. Slide set. London (UK): National Institute for Health and Clinical Excellence; 2008. 18 p. (Clinical guideline; no. 73). Electronic copies: Available in Portable Document Format (PDF) from the NICE Web site.
- Chronic kidney disease. Audit support. London (UK): National Institute for Health and Clinical Excellence; 2008. 19 p. (Clinical guideline; no. 73). Electronic copies: Available in Portable Document Format (PDF) from the NICE Web site.
- The guidelines manual 2007. London (UK): National Institute for Health and Clinical Excellence (NICE); 2007 April. Electronic copies: Available in Portable Document Format (PDF) from the National Institute for Health and Clinical Excellence (NICE) Web site.

Print copies: Available from the National Health Service (NHS) Response Line 0870 1555 455. ref: N1686. 11 Strand, London, WC2N 5HR.

Additional accompanying guideline materials can be found from the National Institute for Health and Clinical Excellence (NICE) Web site.

## PATIENT RESOURCES

The following is available:

- Identifying and treating long-term kidney problems (chronic kidney disease). Understanding NICE guidance - Information for people who use NHS services. London (UK): National Institute for Health and Clinical Excellence; 2008

Sep.11 p. (Clinical guideline; no. 73). Electronic copies: Available in English and Welsh from the National Institute for Health and Clinical Excellence (NICE) Web site.

Print copies: Available from the National Health Service (NHS) Response Line 0870 1555 455. ref: N1687. 11 Strand, London, WC2N 5HR.



## NGC STATUS

This summary was completed by ECRI Institute on October 2, 2009.

The National Institute for Health and Clinical Excellence (NICE) has granted the National Guideline Clearinghouse (NGC) permission to include summaries of their clinical guidelines with the intention of disseminating and facilitating the implementation of that guidance. NICE has not yet verified this content to confirm that it accurately reflects that original NICE guidance and therefore no guarantees are given by NICE in this regard. All NICE clinical guidelines are prepared in relation to the National Health Service in England and Wales. NICE has not been involved in the development or adaptation of NICE guidance for use in any other country. The full versions of all NICE guidance can be found at www.nice.org.uk.

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